Significant Progress in the Treatment of Hepatitis C

By Badar Muneer, MD

HEPATITIS C (HCV) is a common cause of liver disease and cirrhosis in the United States. It is the most common indication for liver transplantation, and the cause of more than 50% of hepatocellular carcinoma in the U.S. Most patients with HCV are asymptomatic, and are thus not tested. Diagnosing and treating patients at earlier stages of HCV would be beneficial, and could prevent the development of cirrhosis and its associated complications. The Centers for Disease Control and Prevention (CDC) estimates that without diagnosis and treatment, about 1.7 million HCV patients will develop cirrhosis, more than 400,000 will develop hepatocellular carcinoma, and almost 1 million will die from HCV-related complications. Another benefit of early diagnosis is that patients with less fibrosis respond better to HCV therapy.

The CDC now recommends one-time HCV antibody testing for all individuals born between 1945 and 1965, also known as "Baby Boomers." The prevalence of HCV antibody in this group is five times higher than people born before or after. In fact, 75% of adults with HCV were born in these years. Testing everyone born between 1945 through 1965 would find an estimated 800,000 undiagnosed HCV cases.

TESTING EVERYONE BORN BETWEEN 1945 AND 1965 WOULD FIND AN ESTIMATED 800,000 UNDIAGNOSED HCV CASES.

The standard of care for the treatment of HCV had been combination therapy with pegylated interferon and ribavirin. This therapy had suboptimal sustained virologic response (SVR or cure) rates. In 2011, the FDA approved the first generation of direct-acting antiviral agents (DAAs) for the treatment of genotype 1 HCV. These protease inhibitors (Boceprevir and Telaprevir) in combination with pegylated interferon and ribavirin significantly increased the SVR rates to 68-75% in treatment-naïve white patients, 52-63% in treatment-naïve black patients, and 29-83% in treatment-experienced patients. In addition, these regimens allowed shortening therapy in certain subgroups of patients to only 24 weeks (compared to the standard 48 weeks).

However, there are still many limitations and challenges with Telaprevir and Boceprevir. The discontinuation rate due to severe adverse events is about 10-12%, and even higher in cirrhotic patients (20-25%). Anemia is a major side effect with both Telaprevir and Boceprevir. More than 40% of patients develop anemia requiring dose adjustment of ribavirin with or without the use of erythropoietin. Skin rash is also common with Telaprevir and about 10% of patients stop treatment due to severe skin rash. These side effects are more common in patients with cirrhosis. Drug-drug interactions are also major problems with Telaprevir and Boceprevir. In addition, DAAs are not yet approved for HCV patients co-infected with HIV or hepatitis B, post-liver transplant patients, or patients infected with non-genotype 1 HCV.

The most exciting research ongoing for HCV is the use of interferon-free (and often, ribavirin-free) regimens. The goal of such therapies will be simpler and more effective treatment options for HCV. These will have higher SVR rates, less side effects, purely oral regimens, shorter duration, and will be effective against all HCV genotypes. Currently, there are a multitude of such phase 2 and phase 3 trials being performed. The preliminary data has been excellent with SVR rates as high as 100% with treatment durations as short as 12 weeks.

In summary, significant progress has been made in the treatment of HCV. Although somewhat limited by toxicity and the continued need for interferon, the currently-approved medications are able to cure a majority of patients with HCV. However, in the next 2-5 years, we will likely reach a point of being able to cure almost all patients with shorter, interferon-free, well-tolerated regime.

Dr. Badar Muneer is a transplant hepatologist at University Hospitals Digestive Health Institute and an instructor at Case Western Reserve University School of Medicine. For more information, visit www.uhhospitals.org/transplant.